

# The Impact of Agent Orange Exposure on Bladder Cancer

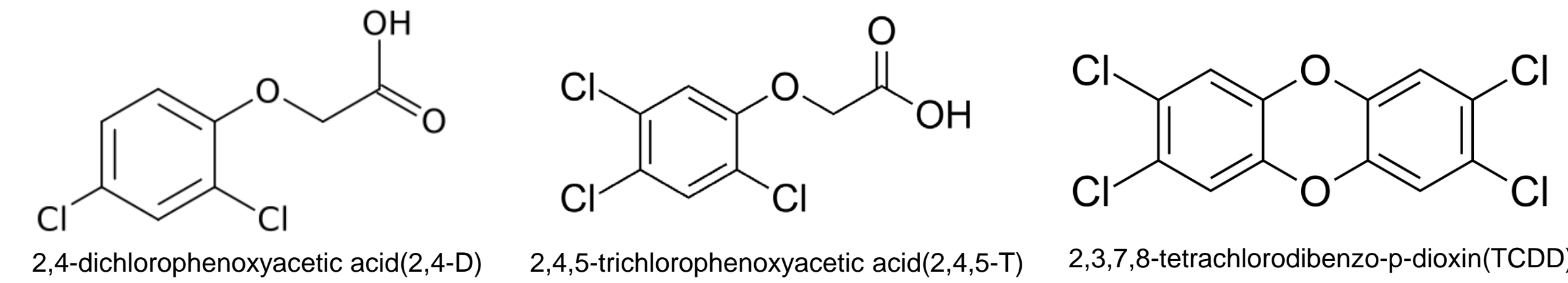
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## Background & Objectives

- Agent Orange (AO) is a mixture of herbicides used during the Vietnam War to clear forest cover that concealed opposition forces and destroy crops



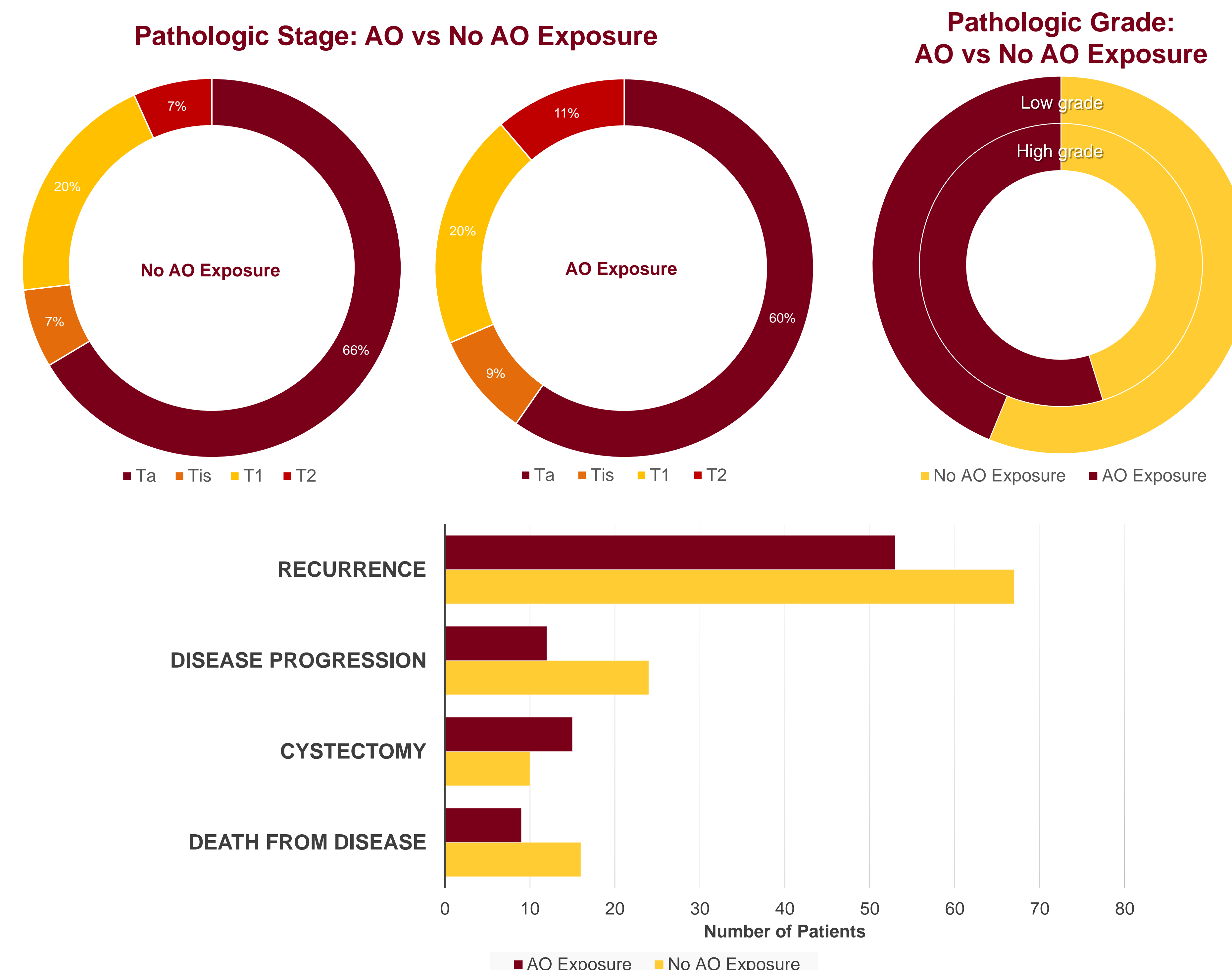
- In 2014, the National Academy of Sciences (previously the Institute of Medicine) reported epidemiologic data that suggested an association between bladder cancer and AO exposure<sup>1</sup>
  - Higher levels of exposure are associated with an approximately 2-fold increase in death from bladder cancer
- Currently there is limited data to explain this observation
- We sought to better characterize our cohort of Vietnam-era veterans with AO exposure and bladder cancer

## Methods

- Vietnam-era veterans who had been diagnosed and/or treated for urothelial carcinoma of the bladder (UCB) at the Minneapolis VA Medical Center were identified
- Medical charts were reviewed to examine
  - Pathologic stage and grade at diagnosis
  - Recurrence
  - Disease progression
  - Cystectomy
  - Death from disease
- Agent Orange exposure was determined by VA registration data
- Patients who left the VA prior to death were censored at date of last cystoscopy; those with muscle-invasion or metastasis were followed beyond this point only to determine if death occurred from UCB

## Results

- 258 patients who met inclusion criteria were identified
- 211 patients with f/u 12 months or greater for evaluation of recurrence and progression
- Median age:** 66 years (range 44-85)
- Median follow-up:** 44 months
- Agent Orange exposure:** 124 patients (48% of cohort)
- AO exposure associated with high-grade disease at presentation (controlling for age and smoking status)
  - OR 2.13 (95% DI 1.264, 3.572, p=0.004)**



Cohort Characteristics			
	Overall	No AO exposure	AO exposure
Pathologic Stage			
Ta	163 (63%)	89 (66%)	74 (60%)
Tis	20 (8%)	9 (7%)	11 (9%)
T1	52 (20%)	27 (20%)	25 (20%)
T2	23 (9%)	9 (7%)	14 (11%)
Pathologic Grade			
High grade	146 (57%)	66 (49%)	80 (65%)
Low grade	112 (43%)	68 (51%)	44 (35%)
Recurrence	130 (62%)	67 (59%)	53 (55%)
Disease progression	36 (17%)	24 (21%)	12 (12%)
Cystectomy	25 (10%)	10 (7%)	15 (12%)
Death from disease	25 (9.7%)	16 (12%)	9 (7%)

Analysis of Risk Factors for High Grade Disease		
	Univariate Analysis	Multivariate Analysis
Agent Orange Exposure	1.8 (p=0.014)	2.13 (p=0.004)
Age	1.05 (p=0.022)	1.07 (p=0.005)
Tobacco use	N/S (p=0.336)	1.53 (p=0.066)

## Conclusions

- In our cohort of Vietnam era veterans with UCB, AO exposure was associated with an approximately 2-fold increased risk of high grade disease at presentation
- Further evaluation in larger cohorts is needed to better understand the mechanism leading to the increased mortality seen in epidemiologic studies

<sup>1</sup>National Academies of Sciences, Engineering, and Medicine. *Veterans and Agent Orange: Update 2014*. Washington, DC: The National Academies Press.